FORM PTO-1390 (Modified) (REV 11-98) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR
2727-154	09/914052

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/01852	03 March 2000 (03.03.00)	01 March 1999 (03.03.99)

TITLE OF INVENTION

Oligomers Substituted by Phosphite Ester, Phosphonic Acid or Carbaborane Functions and the Corresponding PNA Monomers

APPLICANT(S) FOR DO/EO/US

Holger Bock, Thomas Lindhorst

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ A copy of the International Search Report (PCT/ISA/210).
8. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☐ Certificate of Mailing by Express Mail
20. ☐ Other items or information:

Declaration (unsigned)

WIPO publication cover page

EL 905051701 US - Exp. Mail

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/914052	PCT/EP00/01852	2727-154

21. The following fees are submitted:.

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

		CALCULATIONS PTO USE ONLY
☐	Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO and International Search Report not prepared by the EPO or JPO	$970.00
☒	International preliminary examination fee (37 CFR 1.482) not paid to USPTO but Internation Search Report prepared by the EPO or JPO	$840.00
☐	International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	$690.00
☐	International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)	$670.00
☐	International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)	$96.00

ENTER APPROPRIATE BASIC FEE AMOUNT =		$860.00
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).		$0.00

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	10 - 20 =	0	x $18.00	$0.00
Independent claims	1 - 3 =	0	x $78.00	$0.00
Multiple Dependent Claims **(check if applicable)**.			☐	$0.00

TOTAL OF ABOVE CALCULATIONS =		$860.00
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) **(check if applicable)**.	☐	$0.00
SUBTOTAL =		$860.00
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)). +		$0.00
TOTAL NATIONAL FEE =		$860.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) **(check if applicable).**	☐	$0.00
TOTAL FEES ENCLOSED =		$860.00
Amount to be: refunded		$
charged		$

☒ A check in the amount of **$860.00** to cover the above fees is enclosed.

☐ Please charge my Deposit Account No. in the amount of to cover the above fees.
A duplicate copy of this sheet is enclosed.

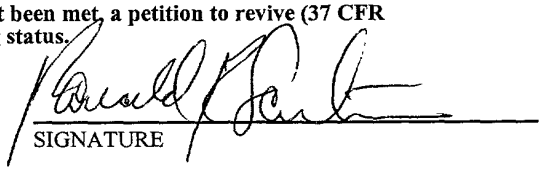
☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **501145** A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Ronald R. Santucci
Pitney, Hardin, Kipp & Szuch, LLP
711 Third Avenue, 20th Floor
New York, New York 10017

(212)687-6000



SIGNATURE

Ronald R. Santucci
NAME

28,988
REGISTRATION NUMBER

August 21, 2001
DATE

2727-154

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Holger Bock, Thomas Lindhorst

Serial No.: Not Yet Assigned

International Appln. No.:PCT/EP00/01852

International Filing Date: 03 March 2000

Priority Date Claimed: 03 March 1999

For: OLIGOMERS SUBSTITUTED BY PHOSPHITE ESTER, PHOSPHONIC ACID OR CARBABORANE FUNCTIONS AND THE CORRESPONDING PNA MONOMERS

PRELIMINARY AMENDMENT

Box PCT
Commissioner for Patents
Washington, D.C. 20231
Attn: DO/EO/US

S I R:

Preliminary to examination of the above-identified application kindly amend the application as follows:

In the Claims:

Kindly rewrite claims 3, 4, 5, 8, 9 and 10 as follows:

3. (Amended) A compound as defined in claim 1, wherein W is a hydrogen atom, U one or more units of formula Y, and Z an OH group.

4. (Amended) A compound as defined in claim 1, wherein at least one of the residues R^1 and R^2 exhibits one or more phosphite ester or phosphonic acid functions.

5. (Amended) A compound as defined in claim 1, wherein at least one of the residues R^1 and R^2 exhibits one or more carbaborane

functions.

8. (Amended) A compound as defined in claim 6, wherein the amine protecting group is an Fmoc, Boc, Cbz, Mmt, or Bhoc protecting group.

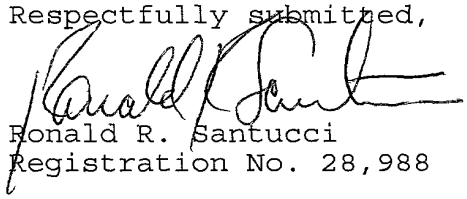
9. (Amended) A process for the production of a compound as defined in claim 1, wherein compounds as defined in claim 6 are converted in known manner.

10. (Amended) A method of using a compound as defined in claim 1 for cancer therapy.

REMARKS

The claims of the above-identified application have been amended to remove all multiple dependencies. No new matter has been added. Accordingly, an early examination of the application is respectfully requested.

Respectfully submitted,



Ronald R. Santucci
Registration No. 28,988

Pitney, Hardin, Kipp & Szuch, LLP
711 Third Avenue, 20th Floor
New York, New York 10017
212-687-6000

APPENDIX:

3. (Amended) A compound as defined in [claim 1 or claim 2] claim 1, wherein W is a hydrogen atom, U one or more units of formula Y, and Z an OH group. .

4. (Amended) A compound as defined in [any of the previous claims] claim 1, wherein at least one of the residues R^1 and R^2 exhibits one or more phosphite ester or phosphonic acid functions.

5. (Amended) A compound as defined in [any of the previous claims] claim 1, wherein at least one of the residues R^1 and R^2 exhibits one or more carbaborane functions.

8. (Amended) A compound as defined in [claim 6 or claim 7] claim 6, wherein the amine protecting group is an Fmoc, Boc, Cbz, Mmt or Bhoc protecting group.

9. (Amended) A process for the production of a compound as defined in [any of claims 1 to 5] claim 1, wherein compounds as defined in [any of claims 6 to 8] claim 6 are converted in known manner.

10. (Amended) A method of using a compound as defined in [any of claims 1 to 5] claim 1 for cancer therapy.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Holger Bock and Thomas Lindhorst
Serial No.	:	09/914,052
For	:	OLIGOMERS SUBSTITUTED BY PHOSPHITE ESTER, PHOSPHONIC ACID OR CARBABORANE FUNCTIONS AND THE CORRESPONDING PNA MONOMERS
Filed	:	
Int'l Appln. No.	:	PCT/EP00/01852
Int'l Filing Date	:	03 March 2000 (03.03.00)
Priority Date	:	03 March 1999 (03.03.99)
Examiner	:	Not Yet Assigned
Art Unit	:	Not Yet Assigned

745 Fifth Avenue
New York, NY 10151

SECOND PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

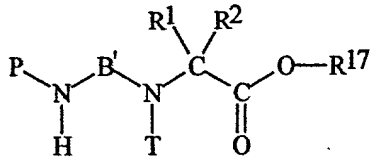
Dear Sir:

Prior to the examination of the above referenced application, Applicants respectfully request that the application be further preliminarily amended as follows:

In the Claims:

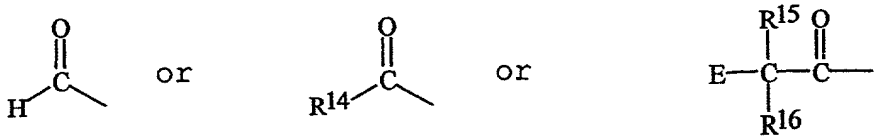
Kindly rewrite claims 6 and 9 as follows:

6. (Amended) A compound of the general formula II



II

in which T is hydrogen or a group of the formula



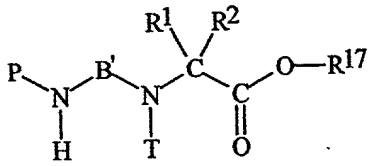
the residue R^{17} is hydrogen or allyl, benzyl, ethyl, methyl, 2,2,2-trichloro-tert-butyl, 2,2,2-trichloroethyl, α-chloro-(trifluoromethyl)benzyl, 2-(p-toluenesulfonyl)ethyl, diphenyl-methyl, 2-(trimethylsilyl)ethyl, methoxymethyl, (2-trimethyl-silyl)ethoxymethyl, benzyloxymethyl, or (2-methoxy) ethyloxymethyl,

the residue P is hydrogen or an amine protecting group,

the residue R^{14} is a group of the formula CH_nX_{3-n} (n = 0 to 3, X = F, Cl, Br, I), a phenyl group, or a *p*-methoxyphenyl group, and

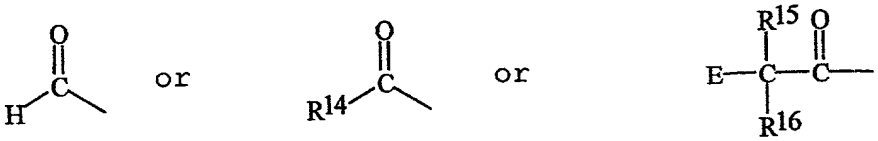
B′, E, the residues R^1 and R^2, and R^{15} and R^{16} have the meanings stated in claim 1.

9. (Twice Amended) A process for the production of a compound as defined in claim 1, wherein compounds of the general formula II



II

in which T is hydrogen or a group of the formula



the residue R^{17} is hydrogen or allyl, benzyl, ethyl, methyl, 2,2,2-trichloro-tert-butyl, 2,2,2-trichloroethyl, α-chloro-(trifluoromethyl)benzyl, 2-(p-toluenesulfonyl)ethyl, diphenyl-methyl, 2-(trimethylsilyl)ethyl, methoxymethyl, (2-trimethyl-silyl)ethoxymethyl, benzyloxymethyl, or (2-methoxy)ethyloxymethyl,

the residue P is hydrogen or an amine protecting group,

the residue R^{14} is a group of the formula CH_nX_{3-n} (n = 0 to 3, X = F, Cl, Br, I), a phenyl group, or a *p*-methoxyphenyl group, and

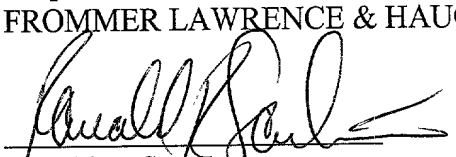
B', E, the residue R^1 and R^2, and R^{15} and R^{16} have the meanings stated in claim 1 are converted in known matter.

REMARKS

Consideration of the application as further preliminarily amended is respectfully requested. The claims have been amended to remove multiple dependencies. No new matter has been added. Accordingly, an early examination of the application is respectfully requested.

The Commissioner is authorized to charge any additional fees that may be required to Deposit Account No. 50-0320.

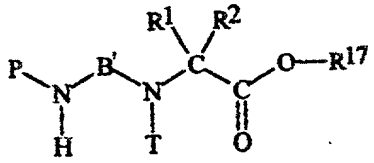
Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: 

Ronald R. Santucci
Reg. No. 28,988
(212) 588-0800

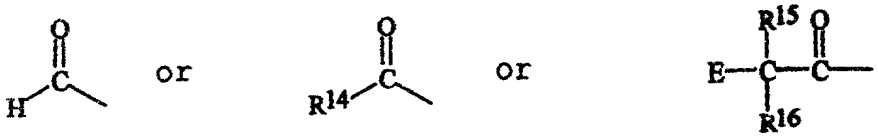
APPENDIX (with claim markings):

6. (Amended) A compound of the general formula II



II

in which T is hydrogen or a group of the formula



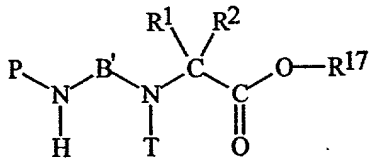
the residue R^{17} is hydrogen or allyl, benzyl, ethyl, methyl, 2,2,2-trichloro-tert-butyl, 2,2,2-trichloroethyl, α-chloro-(trifluoromethyl)benzyl, 2-(p-toluenesulfonyl)ethyl, diphenyl-methyl, 2-(trimethylsilyl)ethyl, methoxymethyl, (2-trimethyl-silyl)ethoxymethyl, benzyloxymethyl, or (2-methoxy) ethyloxymethyl,

the residue P is hydrogen or an amine protecting group,

the residue R^{14} is a group of the formula CH_nX_{3-n} (n = 0 to 3, X = F, Cl, Br, I), a phenyl group, or a *p*-methoxyphenyl group, and

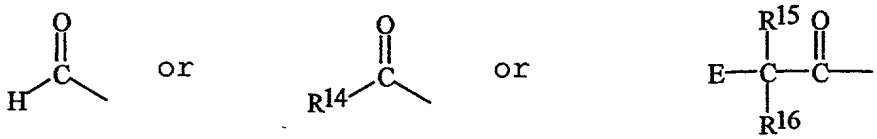
B', E, the residues R^1 [und] and R^2, and R^{15} [und] and R^{16} have the meanings stated in [claims 1 to 5] claim 1.

9. (Twice Amended) A process for the production of a compound as defined in claim 1, wherein compounds of the general formula II



II

in which T is hydrogen or a group of the formula



the residue R^{17} is hydrogen or allyl, benzyl, ethyl, methyl, 2,2,2-trichloro-tert-butyl, 2,2,2-trichloroethyl, α-chloro-(trifluoromethyl)benzyl, 2-(p-toluenesulfonyl)ethyl, diphenyl-methyl, 2-(trimethylsilyl)ethyl, methoxymethyl, (2-trimethyl-silyl)ethoxymethyl, benzyloxymethyl, or (2-methoxy)ethyloxymethyl,

the residue P is hydrogen or an amine protecting group,

the residue R^{14} is a group of the formula CH_nX_{3-n} (n = 0 to 3, X = F, Cl, Br, I), a phenyl group, or a *p*-methoxyphenyl group, and

B', E, the residue R^1 and R^2, and R^{15} and R^{16} have the meanings stated in claim 1 [wherein compounds as defined in claim 6] are converted in known matter.

Oligomers substituted by phosphite ester, phosphonic acid, or carbaborane functions and the corresponding PNA monomers

The invention relates to novel oligomers containing PNA units substituted by phosphite ester, phosphonic acid, or carbaborane functions, and to PNA monomers substituted by phosphite ester, phosphonic acid, or carbaborane functions, from which the novel oligomers are produced.

It is known that peptidonucleic acids (PNAs) can bind to complementary nucleic acids (DNA or RNA) with greater affinity than their natural prototypes (M. Egholm, O. Buchardt, L. Christensen, C. Behrens, S.M. Freier, D.A. Driver, R.H. Berg, S.K. Kim, B. Norden, P.E. Nielsen, *Nature*, **1993**, 365, 566-568, B. Hyrup, P.E. Nielsen, *Bioorg. Med. Chem.*, **1996**, 4, 5-23).

However, the ability of hitherto known PNA oligomers to permeate into cells is very low compared with DNA or RNA. The usefulness of PNAs as antisense agents is greatly dependent on their intracellular availability, however.

Thus it is the object of the present invention to provide oligomers which, like PNAs, can bind to DNAs or RNAs whilst exhibiting improved ability to permeate into cells.

This object is achieved in the present invention by compounds of the formula

W-U-Z

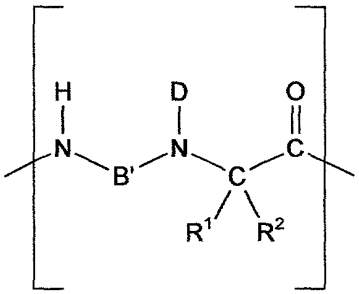
in which W may be a hydrogen atom or an amino acid unit or PNA unit.

U contains at least one unit of the formula Y and possibly one or more amino acid units and/or PNA units.

Z can be an OH function, an amino acid unit, or a PNA unit.

The inventors have found that the introduction of one or more phosphonic acid functions or phosphite ester functions, in particular, but alternatively the introduction of one or more carbaborane functions, into the side chain increases the cell-permeating ability of the PNA oligomers.

Y is a unit of the formula:

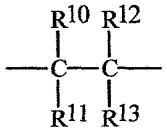


Y

,

in which

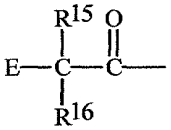
B' denotes a group of the formula:



,

and

D denotes a group of the formula:



.

The residues R^{10} to R^{13} can independently contain up to 20 carbon atoms, preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms. They can independently be hydrogen atoms, unsubstituted alkyl, alkenyl, alkaryl, aryl, or alicyclic groups, which groups may be branched or unbranched; these residues are preferably hydrogen atoms.

Optionally two of the residues R^{10} to R^{13}, which are separated from each other by up to two carbon atoms, can in each case be components of a common ring system, this ring system being either an alicyclic monocyclic compound (3-8 ring atoms), that is unsubstituted or is substituted by a branched or unbranched C_1-C_5 alkyl group, or a phenyl ring; this ring system is preferably an unsubstituted cyclopentyl, cyclohexyl, or phenyl ring.

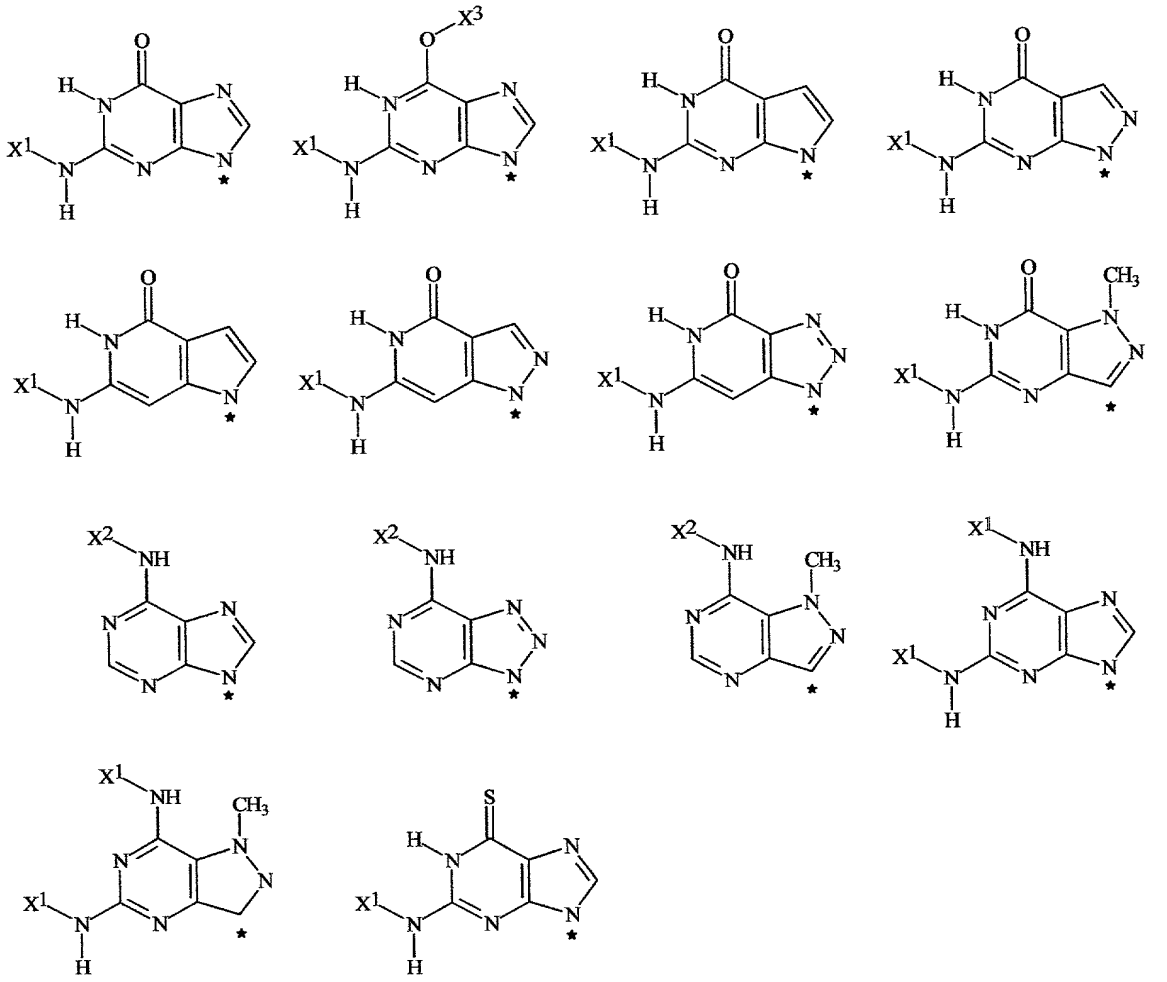
The residues R^{15} and R^{16} can independently contain up to 20 carbon atoms and preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms. They are independently selected from the group comprising hydrogen atoms and unsubstituted alkyl, alkenyl, alkaryl, aryl, or alicyclic groups, said groups being branched or unbranched; more preferably, these residues are hydrogen atoms.

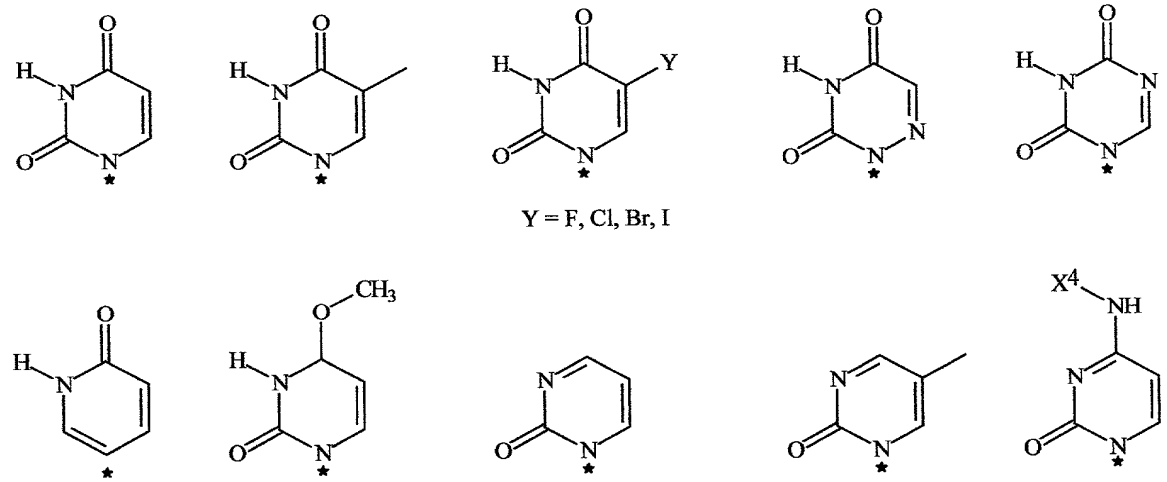
The residues R^{15} and R^{16} can optionally be components of a common ring system, this ring system being an alicyclic monocyclic compound (3-6 ring atoms) that is unsubstituted or substituted by a branched or unbranched C_1-C_5 alkyl group. This ring system is preferably an unsubstituted cyclohexyl ring or a cyclopentyl ring.

Throughout this application, the alkyl groups can be, for example, methyl, ethyl, propyl, or butyl groups.

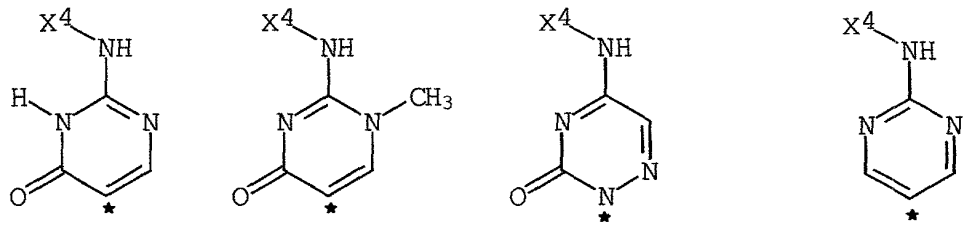
E can be a natural or synthetic nucleobase optionally substituted by protecting groups, such as X^1 to X^4. Such nucleobases are capable of forming Watson-Crick or Hoogsteen base pairs.

Preferably, E can be a group of one of the following formulas:





Y = F, Cl, Br, I



★ substitution site

in which X^1 to X^4 can independently be hydrogen atoms or one of the following substituents known from the technology of protecting groups for nucleobases:

X^1, X^2, and X^4: acetyl (Ac), isobutyryl (iBu-CO), carbobenzoxy (Cbz), (4-methoxyphenyl)diphenylmethyl (Mmt), benzhydryloxycarbonyl (Bhoc), and anisoyl (An), 4-*tert*-butylbenzoyl (tBuBz).

X^3: benzyl (Bn), diphenylcarbamoyl (Dpc).

Most preferably, E is selected from:

N^2-acetylguaninyl, N^2-isobutyrylguaninyl, N^2-benzyloxycarbonylguaninyl, N^2-(4-methoxyphenyl)diphenylmethylguaninyl, N^2-benzhydryloxycarbonylguaninyl, N^6-benzyloxycarbonyladeninyl, N^6-(4-methoxyphenyl)diphenylmethyladeninyl, N^6-anisoyladeninyl, N^6-benzhydryloxycarbonyladeninyl, O^6-benzylguaninyl (X^1 is a hydrogen atom), N^2-acetyl-O^6-diphenylcarbamoylguaninyl, N^2-isobutyryl-O^6-diphenylcarbamoylguaninyl, N^2-benzyloxycarbonyl-O^6-diphenylcarbamoylguaninyl, N^2-(4-methoxyphenyl)diphenylmethyl-O^6-diphenylcarbamoylguaninyl, N^2-benzhydryloxycarbonyl-O^6-diphenylcarbamoylguaninyl, N^4-benzyloxycarbonylcytosinyl, N^4-(4-methoxyphenyl)diphenylmethylcytosinyl, N^4-4-*tert*-butylbenzoylcytosinyl, N^4-benzhydryloxycarbonylcytosinyl, N^2-benzyloxycarbonyl-pseudoisocytosinyl, N^2-(4-methoxyphenyl)diphenylmethyl-pseudoisocytosinyl, N^2-4-*tert*-butylbenzoyl-pseudoisocytosinyl, N^2-benzhydryloxycarbonyl-

pseudoisocytosinyl, adeninyl, cytosinyl, pseudoisocytosinyl, guaninyl, thyminyl, or uracinyl residue.

Most preferably, E is an adeninyl, cytosinyl, pseudoisocytosinyl, guaninyl, thyminyl, or uracilyl residue.

The residues R^1 and R^2 can independently be H-substituted alkyl, alkenyl, alkaryl, aryl, or alicyclic groups containing up to 20 carbons, whilst at least one of the residues R^1 or R^2 exhibits one or more phosphite ester, phosphonic acid, or carbaborane functions.

Phosphonic acid functions can have, for example, the formula $-P(=O)(OH)_2$.

Phosphite ester functions can have, for example, the formula $-P(=O)(OV)_2$ or $P(=O)(OV)(OH)$. V can be an unsubstituted alkyl, alkenyl, alkaryl, aryl, or alicyclic group containing up to 20 carbons, more preferably up to 7 carbon atoms, and is most preferably a methyl, ethyl, or benzyl group.

Carbaborane functions containing up to 20 boron atoms - in particular up to 12, 10 or 8 boron atoms - and from 1 to 4 carbon atoms are preferred, known carbaborane functions being particularly preferred.

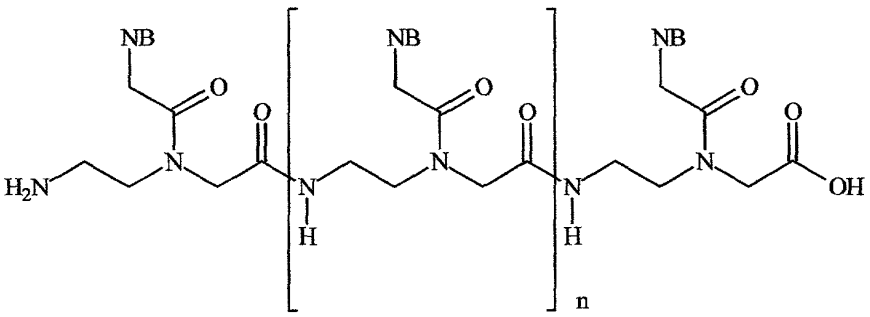
Preferably, the residues R^1 or R^2 contain 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms and are defined as above.

The residues R^1 and R^2 can be branched or unbranched. Most preferably, the residues R^1 and R^2 are defined as above whilst at least one of R^1 and R^2 is or contains a substituent of a synthetic amino acid.

Very preferably, the residues R^1 and R^2 are independently selected from the group comprising hydrogen atoms and units of formu-

las $-CH_2-[P(=O)(O-K)_3]$ and $-CH_2-C(CH_3)_2-[P(=O)(O-K)_2]$, K being a hydrogen atom or a methyl, ethyl, or benzyl group.

PNAs are optionally substituted oligomers having a *N*-(2-aminoethyl)glycine backbone. The substituent NB is a nucleobase.



PNA oligomers are produced by linking peptide bonds between substituted *N*-acetyl-*n*-(2-aminoethyl)glycine building blocks (PNA monomers). In the oligomer, each of these substituted *N*-acetyl-*n*-(2-aminoethyl)glycine building blocks is a PNA unit. In the present invention, PNA units known *per se* can be used, units of the above formula being preferred.

Preferably, the compound W-U-Z is composed of up to 50, more preferably up to 40, and most preferably up to 30, of these units W, U and Z. For example, such compounds W-U-Z can contain up to 5 units of formula W, up to 30 units of formula U and up to 10 units of formula Z.

More preferably, W is a hydrogen atom, U comprises one or more units of formula Y and one or more PNA units, and Z is an OH group.

Most preferably, W is a hydrogen atom, U one or more units of formula Y, and Z an OH group.

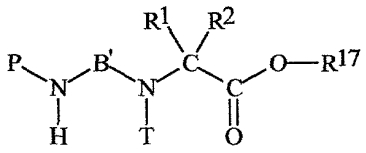
If the oligomers contain carbaborane functions, they can be used in a boron neutron capture therapy (BNCT) for controlling cancerous tumors. BNCT involves the transfer of boron-containing

molecules into cancer cells. The cells are then bombarded with slow neutrons, by which means the boron atoms decompose to high-energy particles and irreversibly destroy the surrounding tissue (*Chemie in unserer Zeit* **1997**, *31st Year of Issue No. 5*, 235). In BNCT work, boron-containing amino acids, sugars, porphyrins, phospholipides, thiouracil derivatives, nucleotide analogs, and nucleosides have been synthesized and examined (M. F. Hawthorne, *Angew. Chem.* ***1993***, *105*, 997).

In the present invention, U can be an oligopeptide made up of amino acid units and/or PNA units and at least one unit of formula Y linked together in any order.

The oligomers of the invention can be produced, for example, by means of processes described in the literature by conversion of compounds of the general formula **II** in known manner (*eg*, L. Christensen, R. Fitzpatrick, B. Gildea, K.H. Petersen, H.F. Hansen, T. Koch, M. Egholm, O. Buchaedt, P.E. Nielsen, J. Coull, R.H. Berg, *J.Pept.Sci.* **1995**, 1, 175-183, T. Koch, H.F. Hansen, P. Andersen, T. Larsen, H.G. Batz, K. Otteson, H. Oerum, *J.Pept.Res.* ***1997***, 49, 80-88, F. Bergmann, W. Bannwarth, S. Tam, *Tetrahedron Lett.* **1995**, 36, 6823-6826)

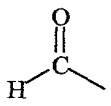
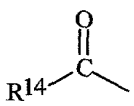
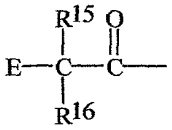
In the compounds of the general formula **II**



II

B' is as defined above,

T is a hydrogen atom or a group of the formula

 or  or 

The residue R^{17} can be a hydrogen atom or an allyl, benzyl, ethyl, methyl, 2,2,2-trichloro-*tert*-butyl, 2,2,2-trichloroethyl, α-chloro(trifluoromethyl)benzyl, 2-(*p*-toluenesulfonyl)ethyl, diphenylmethyl, 2-(trimethylsilyl)ethyl, methoxymethyl, (2-trimethylsilyl)ethoxymethyl, benzyloxymethyl, or (2-methoxy)ethyloxymethyl group.

When the residue R^{17} is not a hydrogen atom, it can be bound to a solid phase. A suitable solid phase comprises any conventional solid-phase resin as used in organic solid-phase synthesis, and polystyrene-divinylbenzene resins, polyethylene glycol resins or polyethylene glycol polystyrene resins are preferred.

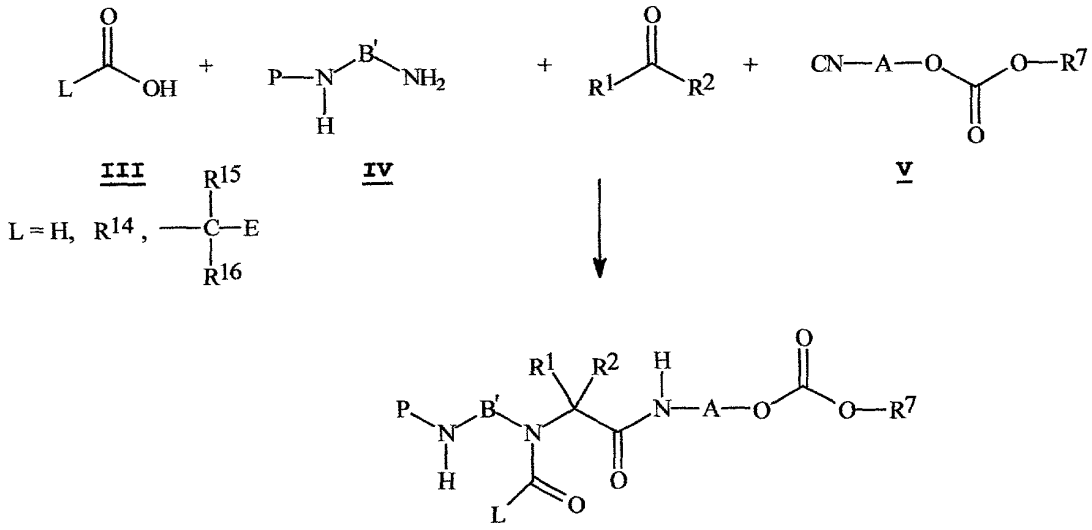
P can be a hydrogen atom or a cleavable amine protecting group. The amine protecting group must be selectively cleavable in the presence of the nucleobase protecting groups X^1 to X^4. Preferably, P is a hydrogen atom, an oxocarbamate or thiocarbamate protecting group, and more preferably, a hydrogen atom or an Fmoc, Boc, Cbz, Mmt or Bhoc protecting group.

The residue R^{14} can be a group of formula CH_nX_{3-n} (n = 0 to 3, X = F, Cl, Br, I), phenyl or *p*-methoxyphenyl.

E, the residues R^1 and R^2, and R^{15} and R^{16} have the meanings stated above.

The compounds of the general formula **II** can, for example, be produced from compounds of the general formula **I** by known methods (PCT/EP 98/04622).

The synthesis of compounds of the general formula **I** is effected by means of the Ugi reaction (U 4CR), for example, according to the following reaction diagram:



III IV V

I

The reaction can be carried out, for example, as described in the literature (I. Ugi *et al.*, Chem. Ber., **1961**, 94, 2802).

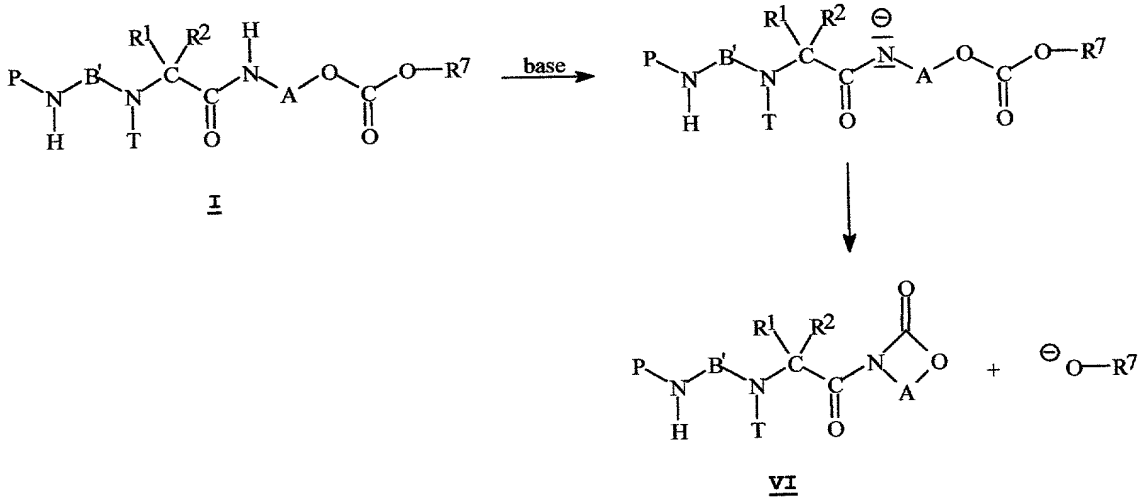
The nucleobase acetic acid components E-C($R^{15}R^{16}$)-COOH are produced as described in the literature (E. Uhlmann, A. Peyman, G. Breipohl, D.W. Will, *Angew. Chem.*, **1998**, 110, 2954-2983).

The amine components of the general formula **IV** are produced, eg, by the Krapcko method (A.P. Krapcko, C.S. Kuile, *Synthetic Communications*, **1990**, 20(16), 2559-2564).

The isocyanide components of the general formula **V** can be produced by any of the processes disclosed in Patent Application PCT/EP 98/04622. The processes are suitable for both resin-bonded isocyanide components and non-resin-bonded isocyanide components.

The compounds of the general formula **I** are then converted, *eg* by the process described in the literature (Th. Lindhorst, H. Bock, I. Ugi, *Tetrahedron* **1999**, *55*, 7411-7420; PCT/EP 98/04622) to give the compounds of the general formula **II**. This is carried out, *eg*, by the addition of an equimolar amount of a nucleophilic base, such as potassium *tert*-butanolate, to the compounds of the

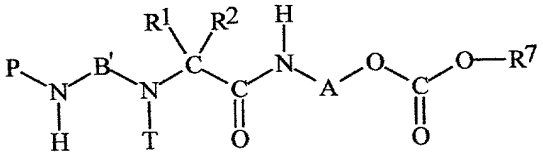
general formula **I** in an aprotic solvent, for example as demonstrated by the following diagram:



I

VI

In the compounds of the general formula **I**



I

,

the groups B', T, P, and residues R^1 und R^2 have the same meanings as stated for the compounds of the general formula **II**.

The residue R^7 has the same meaning as stated for residue R^{17} in the compound of the general formula **II** or may be a phenyl group but not a hydrogen atom.

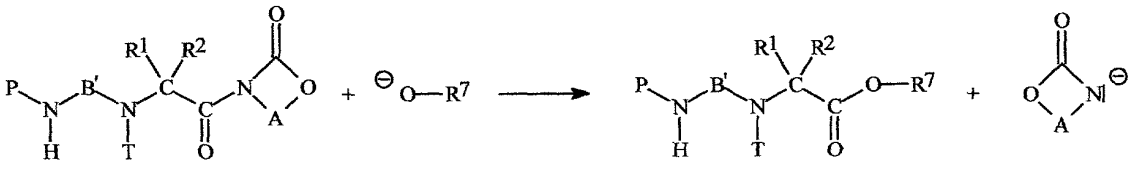
A can be a group of the formula $-C(R^3,R^4)-C(R^5,R^6)-$, in which the residues R^3 to R^6 are independently hydrogen, phenyl, or methyl.

This process is particularly well suited for the generation of novel PNA monomers whose side chains correspond to those of unnatural amino acids. Hitherto known procedures involved the ela-

borate production of the synthetic amino acid for this purpose. Following basic cleavage of the C-terminal protecting group, the base-stable protecting group P can be optionally replaced by a base-labile protecting group P (*eg*, Fmoc).

If the residue R^7 lowers the nucleophilicity of the oxygen atom bound thereto (when R^7 is, *eg*, a phenyl group), the intermediate products **VI** are isolable (*cf* Patent Application PCT/EP 98/04622). **VI** can then be converted by mild basic hydrolysis to the compounds of the general formula **II**, in which R^{17} is a hydrogen atom.

If, in the compounds of the general formula I, the residue R^7 does not lower the nucleophilicity of the oxygen atom bound thereto, the intermediate products **VI** are not isolable. In such cases, **VI** reacts *in situ* with the alkoxides (Alkoholation) formed by the intramolecular ring closure to give the corresponding esters of the general formula **II**, for example as shown by the following diagram.

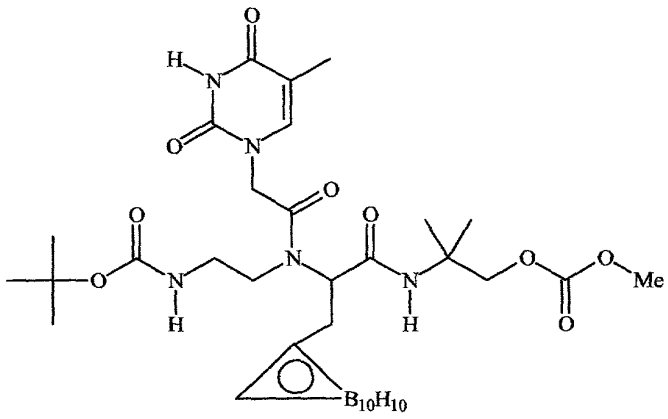


VI **II**

Following the basic cleavage of the C-terminal protecting group, it is possible to remove a base-stable protecting group P as defined above (*eg*, Boc) in the compounds of the general formula **II** by commonly used methods and to optionally replace it by a new protecting group selectively cleavable in the presence of the nucleobase protecting groups X^1 to X^4 (*eg*, the base-labile protecting group Fmoc).

Beispiele:

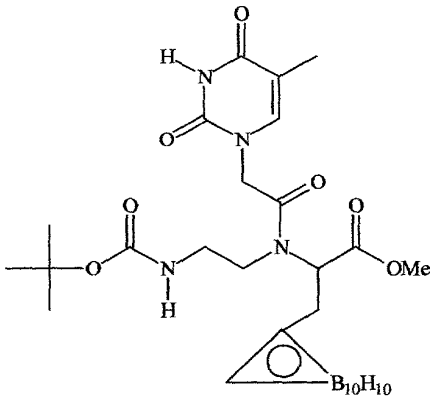
Example 1: Production of



5 mmol each of thyminyl acetic acid, 2-(1,2-dicarbaclosododecaborone)ethanal, *N*-Boc ethylene diamine, and methyl 2-isocyano-2,2-(dimethyl)ethylcarboxylate are dissolved in 50 mL of trifluoroethanol and stirred at 25°C. On completion of the reaction, the solvent is removed.

The reaction mixture is purified by column chromatography. The reaction product is obtained in 70 % yield.

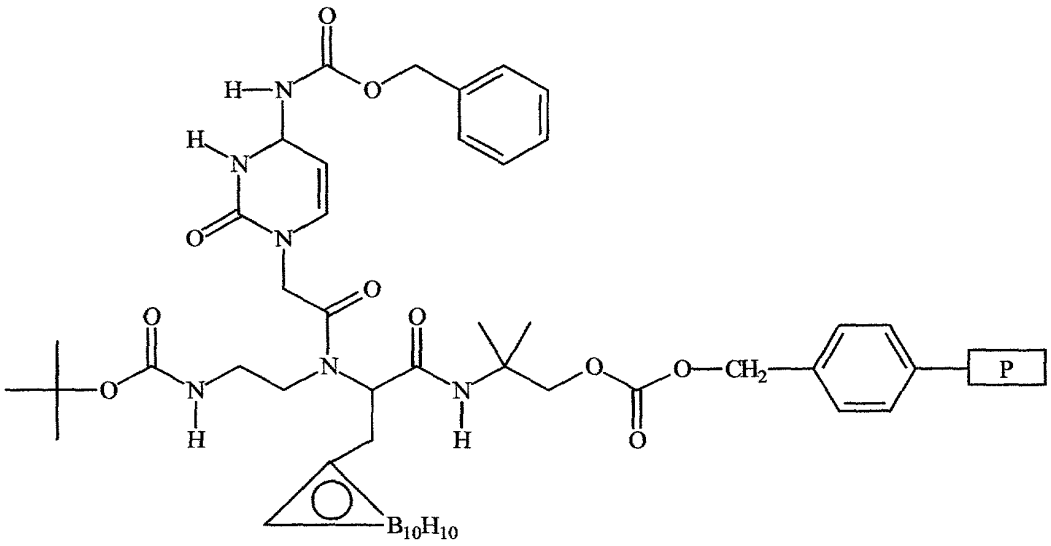
Example 2: Production of



2 mmol of the reaction product of Example 1 are dissolved in 10 mL of absolute THF, and 2 mmol of sodium hydride are added at

25°C. On completion of the reaction, the reaction mixture is filtered through a short silica gel column. The solvent is removed and the reaction product purified by column chromatography. The reaction product is obtained in a yield of 70 %.

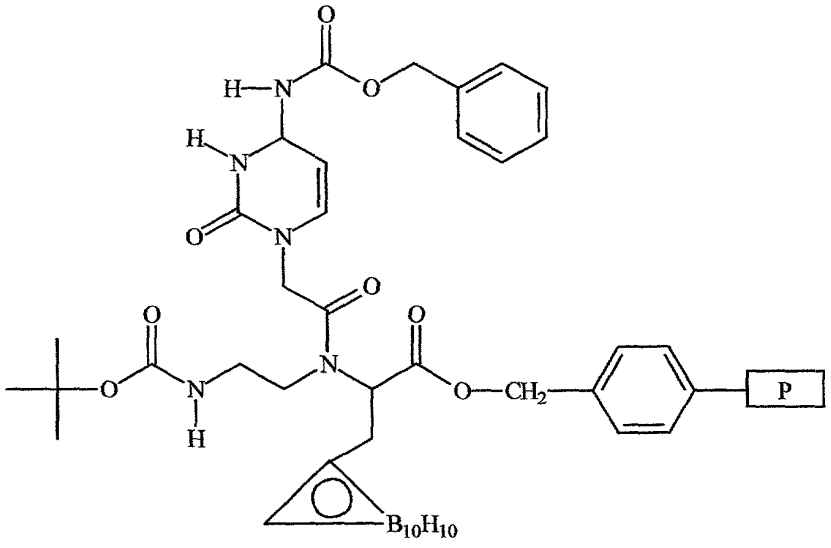
Example 3: Production of



5 mmol each of (N^4-Cbz-cytosyl) acetic acid, 2-(1,2-dicarbaclosododecaborane)ethanal, N-Boc ethylene diamine, and methylpolystyrene 2-isocyano-2,2-(dimethyl)ethylcarboxylate are suspended in 50 mL of trifluoroethanol and stirred at 25°C. On completion of the reaction, the solvent is removed via a frit and the reaction mixture washed a number of times with methanol, dichloromethane, a pH 9 sodium hydrogencarbonate solution, and water.

The reaction product is obtained in a yield of 80 % (determine by bromometric detection of unconverted isocyanide resin).

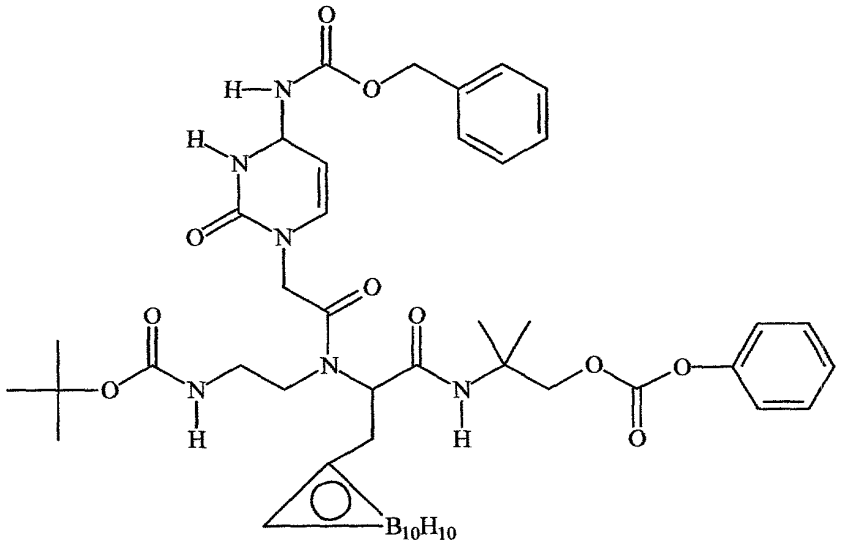
Example 4: Production of



2 mmol of the reaction product of Example 3 are suspended in 10 mL of absolute THF, and 2 mmol of potassium *tert*-butanolate are added at 25°C. On completion of the reaction, the solvent is removed via a frit and the reaction mixture washed a number of times with methanol, dichloromethane, a pH 9 sodium hydrogencarbonate solution, and water.

The reaction product is obtained in a yield of 60 %.

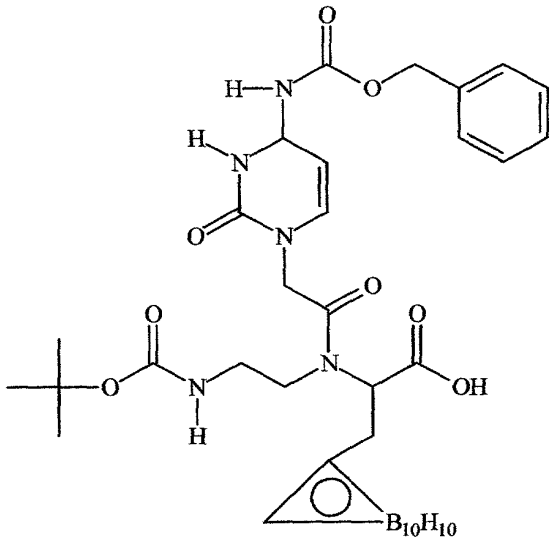
Example 5: Production of



5 mmol each of (N^4-Cbz-cytosyl) acetic acid, 2-(1,2-dicarbaclosododecaborane)ethanal, N-Boc ethylene diamine, and phenyl 2-isocyano-2,2-(dimethyl)ethylcarboxylate are dissolved in 50 mL of trifluoroethanol and stirred at 25°C. On completion of the reaction, the solvent is removed.

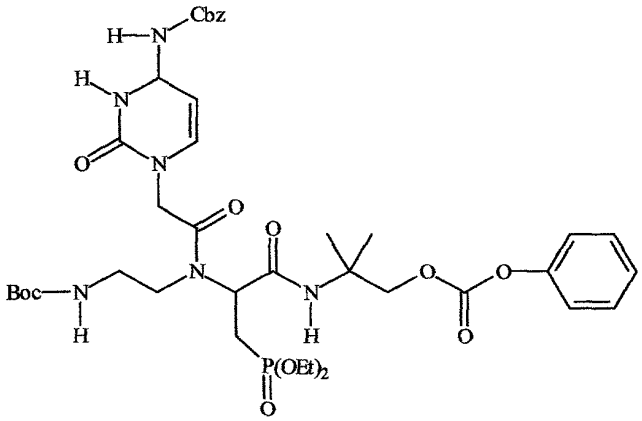
The reaction mixture is purified by column chromatography. The reaction product is obtained in 80 % yield.

Example 6: Production of



2 mmol of the reaction product of Example 5 are dissolved in 10 mL of absolute THF, and 2 mmol of potassium *tert*-butanolate are added at 25°C. On completion of the reaction, an aqueous 1M potassium hydroxide solution is added to the reaction mixture, which is stirred until no more conversion can be detected. The reaction solution is neutralized and the solvent removed. The reaction product is purified by column chromatography. The reaction product is obtained in a yield of 70 %.

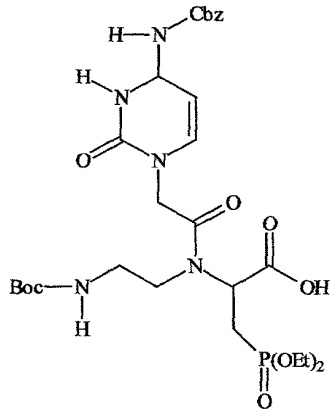
Example 7: Production of



5 mmol each of (N^4-Cbz-cytosyl) acetic acid, diethyl 2-phosphite ester ethanal, N-Boc ethylene diamine, and phenyl 2-isocyano-2,2-(dimethyl)ethylcarboxylate are dissolved in 50 mL of ethanol. In order to improve the solubility properties of (N^4-Cbz-cytosyl) acetic acid, 5 mmol of triethylamine are added and the mixture is stirred at 25°C. On completion of the reaction, the solvent is removed.

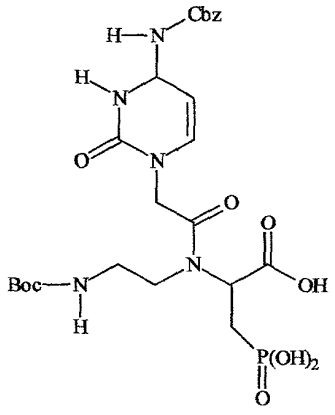
The reaction mixture is purified by column chromatography. The reaction product is obtained in 70 % yield.

Example 8: Production of



2 mmol of the reaction product of Example 7 are dissolved in 10 mL of absolute THF, and 2 mmol of potassium *tert*-butanolate are added at 25°C. On completion of the reaction, 2 mmol of potassium hydroxide as aqueous 1M solution are added to the reaction mixture, which is stirred until no more conversion can be detected. The reaction solution is neutralized and the solvent removed. The reaction product is purified by column chromatography. The reaction product is obtained in a yield of 55 %.

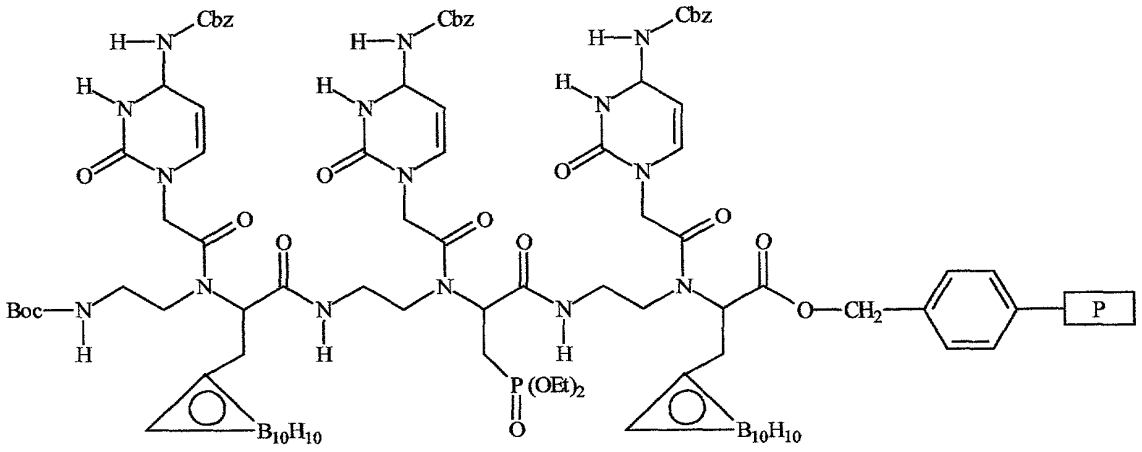
Example 9: Production of



2 mmol of the reaction product of Example 8 are dissolved in 10 mL of absolute THF, and 2 mmol of potassium hydroxide as aqueous 1M solution are added at 50°C. On completion of the reaction, the reaction solution is neutralized and the solvent removed.

The reaction product is purified by preparative HPLC. The reaction product is obtained in a yield of 40 %.

Example 10: Preparation of



Synthesis procedure:

Step 1: 100 mg of the reaction product of Example 4 are presoaked in dichloromethane for 12 h,

Step 2: deprotection with *tert*-butyloxycarbonyl in a peptide synthesizer using a 50% strength solution of trifluoroacetic acid in dichloromethane (1:1 v/v, 2 ml, 1 x 2 minutes, 1 x 30 min),

Step 3: washing with dichloromethane (2 ml, 4 x 20 seconds),

Step 4: neutralization with DIPEA/dichloromethane (1:19 v/v, 2 ml, 2 x 3 min),

Step 5: washing with dichloromethane (2 ml, 2 x 20 seconds), washing with DMF (2 ml, 3 x 20 seconds),

Step 6: addition of 4 equivalents of HBTU and diethylcyclohexylamine in DMF/pyridine (1:1 v/v) und 4 equivalents of the reaction product of Example 8,

Step 7: washing with DMF (2 ml, 3 x 20 seconds) und dichloromethane (3 ml, 3 x 20 seconds),

Step 8: capping with a solution of 0,5 M acetic anhydride/0,5 M DMF,

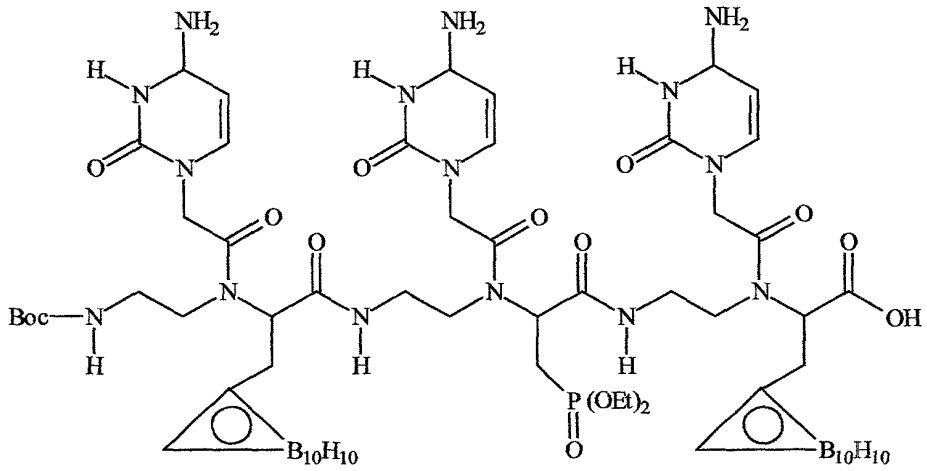
Step 9: washing with DMF (2 ml, 3 x 20 seconds) und dichloromethane (3 ml, 3 x 20 seconds),

Step 10: repetition of the synthesis cycle from Step 2, while in Step 6 4 equivalents of the reaction product of Example 6 are used instead of the reaction product of Example 8,

Step 11: drying in a stream of nitrogen.

The product is obtained in a yield of 97%.

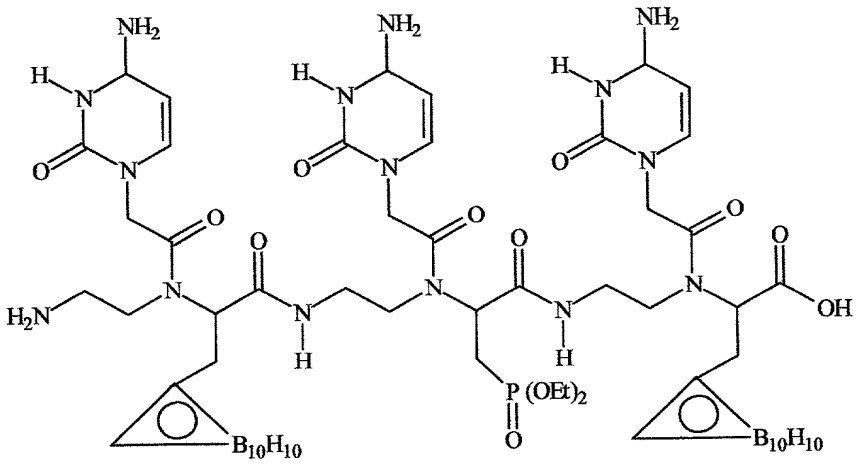
Example 11: Production of



The reaction product of Example 10 is suspended in methanol, and a catalytic amount of platinum-on-carbon is added. The reaction mixture is hydrogenated under a blanket of hydrogen.

On completion of the reaction, the solvent is removed, and the product is purified by preparative HPLC. The reaction product is obtained in a yield of 96 %.

Example 12: Production of



The reaction product of Example 11 is suspended in dichloromethane. There are added 1 mL each of trifluoroacetic acid and thiophenol. On completion of the reaction, the reaction product is purified by preparative HPLC. The reaction product is obtained in a yield of 99 %.

Claims

1. **A compound of the formula**

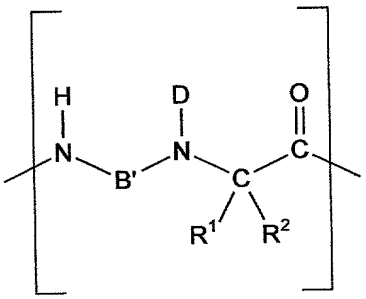
W-U-Z

in which W is a hydrogen atom, an amino acid unit, or a PNA unit,

U contains at least one unit of the formula Y and, optionally, one or more amino acid and/or PNA units,

Z is an OH function, an amino acid unit, or a PNA unit,

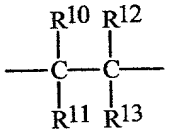
Y is a unit of the formula



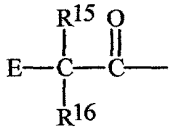
Y

in which

B' is a group of the formula,



D is a group of the formula



,

the residues R^{10} to R^{13} independently contain up to 20 carbon atoms and independently denote hydrogen atoms or unsubstituted alkyl, alkenyl, alkaryl, aryl, or alicyclic groups, said group being branched or unbranched, and optionally two each of the residues R^{10} to R^{13}, separated from each other by up to two carbon atoms, are components of a common ring system, which ring system is either an alicyclic monocyclic compound (3-8 ring atoms), optionally substituted by a branched or unbranched C_{1-5} alkyl group, or a phenyl ring,

the residues R^{15} and R^{16} independently contain up to 20 carbon atoms and independently denote hydrogen atoms or unsubstituted alkyl, alkenyl, alkaryl, aryl, or alicyclic groups, said groups being branched or unbranched, and optionally the residues R^{15} and R^{16} are components of a common ring system, which ring system is an alicyclic monocyclic compound (3-6 ring atoms), optionally substituted by a branched or unbranched C_{1-5} alkyl group,

E is a natural or synthetic nucleobase, optionally substituted by protecting groups and capable of forming Watson-Crick or Hoogsteen base pairs, and

the residues R^1 and R^2 are independently hydrogen atoms, alkyl, alkenyl, alkaryl, aryl, or alicyclic groups containing up to 20 carbons, whilst at least one of the residues R^1 and R^2 exhibits one or more phosphite ester, phosphonic acid, or carbaborane functions.

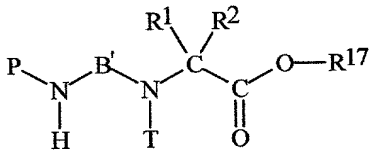
2. A compound as defined in claim 1, comprising a total of up to 50 of the said units W, U and Z.

3. A compound as defined in claim 1 or claim 2, wherein W is a hydrogen atom, U one or more units of formula Y, and Z an OH group.

4. A compound as defined in any of the previous claims, wherein at least one of the residues R^1 and R^2 exhibits one or more phosphite ester or phosphonic acid functions.

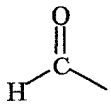
5. A compound as defined in any of the previous claims, wherein at least one of the residues R^1 and R^2 exhibits one or more carbaborane functions.

6. A compound of the general formula **II**

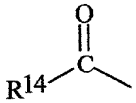


II

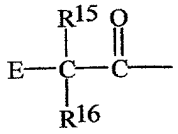
in which T is hydrogen or a group of the formula



or



or



the residue R^{17} is hydrogen or allyl, benzyl, ethyl, methyl, 2,2,2-trichloro-tert-butyl, 2,2,2-trichloroethyl, α-chloro-(trifluoromethyl)benzyl, 2-(p-toluenesulfonyl)ethyl, diphenylmethyl, 2-(trimethylsilyl)ethyl, methoxymethyl, (2-trimethylsilyl)ethoxymethyl, benzyloxymethyl, or (2-methoxy)ethyloxymethyl,

the residue P is hydrogen or an amine protecting group,

the residue R^{14} is a group of the formula CH_nX_{3-n} (n = 0 to 3, X = F, Cl, Br, I), a phenyl group, or a *p*-methoxyphenyl group, and

B', E, the residues R^1 und R^2, and R^{15} und R^{16} have the meanings stated in claims 1 to 5.

7. A compound as defined in claim 6, wherein the residue R^{17} is not a hydrogen atom and is bound to a solid phase.

8. A compound as defined in claim 6 or claim 7, wherein the amine protecting group is an Fmoc, Boc, Cbz, Mmt, or Bhoc protecting group.

9. A process for the production of a compound as defined in any of claims 1 to 5, wherein compounds as defined in any of claims 6 to 8 are converted in known manner.

10. A method of using a compound as defined in any of claims 1 to 5 for cancer therapy.

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DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)

☐ Declaration Submitted with Initial Filing OR ☒ Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required)

Attorney Docket Number	~~2727-154~~ 930008-2006
First Named Inventor	Holger Bock
COMPLETE IF KNOWN	
Application Number	09/914,052
Filing Date	
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Oligomers Substituted by Phosphite Ester, Phosphonic Acid or Carbaborane Functions and the Corresponding PNA Monomers

(Title of the Invention)

the specification of which
☐ is attached hereto
OR
☒ was filed on (MM/DD/YYYY) 03/03/2000 ✓ as United States Application Number or PCT International Application Number PCT/EP00/01852 ✓ and was amended on (MM/DD/YYYY) _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached? YES	NO
DE 199 09 373.3 ✓	Germany ✓	03/03/1999 ✓	☐	☐	☐
			☐	☐	☐
			☐	☐	☐
			☐	☐	☐

☐ Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	
		☐ Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

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DECLARATION — Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application or PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number *(if applicable)*

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

☐ Customer Number → [ ] *Place Customer Number Bar Code Label here*

OR

☒ Registered practitioner(s) name/registration number listed below

Name	Registration Number	Name	Registration Number
Ronald R. Santucci	28,988		

☐ Additional registered practitioner(s) named on supplemental Registered Practitioner Information sheet PTO/SB/02C attached hereto

Direct all correspondence to: ☐ Customer Number or Bar Code Label [ ] *OR* ☒ Correspondence address below

Name	Ronald R. Santucci				
Address	Pitney, Hardin, Kipp & Szuch, LLP				
Address	711 Third Avenue, 20th Floor				
City	New York	State	NY	ZIP	10017
Country	U.S.A.	Telephone	212-687-6000	Fax	212-682-3485

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: ☐ A petition has been filed for this unsigned inventor

Given Name (first and middle [if any])	Family Name or Surname
Holger	Bock

Inventor's Signature	[signature]					Date	Oct. 4th 2001
Residence: City	Munich DEX	State		Country	Germany	Citizenship	German
Post Office Address	Georgenschwaigstr. 38						
Post Office Address	80807 Munich, Germany						
City		State		ZIP		Country	

☒ Additional inventors are being named on the 1 supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto

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DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet
Page 3 of 3

Name of Additional Joint Inventor, if any:	☐ A petition has been filed for this unsigned inventor
Given Name (first and middle [if any])	Family Name or Surname
Thomas	Lindhorst

2-02

Inventor's Signature	/Thomas Lindhorst/					Date	Oct. 4th / 2001
Residence: City	Wasserburg DEX	State		Country	Germany	Citizenship	German
Post Office Address	Unter der Schanz 10						
Post Office Address	83512 Wasserburg, Germany						
City		State		ZIP		Country	

Name of Additional Joint Inventor, if any:	☐ A petition has been filed for this unsigned inventor
Given Name (first and middle [if any])	Family Name or Surname

Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		ZIP		Country	

Name of Additional Joint Inventor, if any:	☐ A petition has been filed for this unsigned inventor
Given Name (first and middle [if any])	Family Name or Surname

Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		ZIP		Country	

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Application

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Washington, D.C. 20231

Application Number	09/914,052
Filing Date	09/914052
First Named Inventor	Holger Bock
Group Art Unit	
Examiner Name	
Attorney Docket Number	930008-2006

Please change the Correspondence Address for the above-identified application to:

☐ Customer Number [ ] → *Type Customer Number here*

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OR

☒ Firm *or* Individual Name	Ronald R. Santucci				
Address	Frommer Lawrence & Haug LLP				
Address	745 Fifth Avenue				
City	New York	State	NY	ZIP	10151
Country	United States of America				
Telephone	212-588-0800	Fax	212-588-0500		

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I am the :

☐ Applicant/Inventor.

☐ Assignee of record of the entire interest.
Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).

☒ Attorney or Agent of record.

☐ Registered practitioner named in the application transmittal letter in an application without an executed oath or declaration. See 37 CFR 1.33(a)(1). Registration Number _____

Typed or Printed Name	Ronald R. Santucci
Signature	
Date	November 20, 2001

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

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Applicant or Patentee: **Holger Bock and Thomas Lindhorst**
Serial or Patent No.: **09/914,052**
Filed or Issued:
For: **"Oligomers Substituted by Phosphite Ester,** Phosphonic Acid or Carbaborane Functions and the Corresponding PNA Monomers"

Frommer Lawrence & Haug LLP
File No.: **930008-2006**

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
(37 CFR 1.9(f) and 1.27(c)) – SMALL BUSINESS CONCERN

I hereby declare that I am

☐ the owner of the small business concern identified below:

☒ an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF CONCERN **Ugichem GmbH**

ADDRESS OF CONCERN **Georgenschwaigstr. 38**
80807 Munich, Germany

I hereby declare that the above-identified small business concern qualifies as a small business concern as defined in 13 CFR 121.12, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled ***"Oligomers Substituted by Phosphite Ester, Phosphonic Acid or Carbaborane Functions and the Corresponding PNA Monomers"*** by inventor(s) **Holger Bock and Thomas Lindhorst** described in

☐ the specification filed herewith.

☒ application serial no. **09/914,052**, filed .

☐ patent no. , issued .

If the rights held by the above-identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37

*NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities (37 CFR 1.27).

Applicant or Patentee: **Holger Bock and Thomas Lindhorst**
Serial or Patent No.: **09/914,052**
Filed or Issued:
For: **"Oligomers Substituted by Phosphite Ester,** Phosphonic Acid or Carbaborane Functions and the Corresponding PNA Monomers"

Frommer Lawrence & Haug LLP
File No.: **930008-2006**

CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Full Name:

Address:

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

Full Name:

Address:

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

Full Name

Address

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Name of Person Signing: Holger Bock

Title in Organization:
(if other than owner)

Address of Person Signing: **Ugichem GmbH**
Georgenschwaigstr. 18
80807 Munich, Germany

Signature: _____ Date: 26th October 2001

United States Patent & Trademark Office

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